

IN THE SPECIFICATION:

Please replace the paragraph spanning page 7, line 18 to page 8, line 9, with the following amended paragraph:

Another embodiment of the present invention relates to a method to identify compounds that regulate myoblast activation and differentiation in a cell. The method includes the steps of: (a) contacting an isolated prelamin A processing-deficient cell with a test compound for regulation of myoblast activation and differentiation; and (b) detecting whether the test compound regulates an activity in the cell selected from the group consisting of: prelamin A processing, prelamin A pre peptide transport, and myoblast activation or differentiation, as compared to in the absence of the test compound. In one aspect, the isolated prelamin A processing-deficient cell is selected from: a cell transfected with a nucleic acid sequence encoding a processing deficient prelamin A protein and a prelamin A processing deficient cell that has been isolated from a patient. In one aspect, the cell is transfected with a nucleic acid sequence encoding a prelamin A protein. In another aspect, the cell is transfected with a nucleic acid sequence encoding a processing-deficient prelamin A protein. In another aspect, the processing-deficient prelamin A is a naturally occurring processing-deficient prelamin A protein. In yet another aspect, the processing-deficient prelamin A is a synthetically created processing-deficient prelamin A protein. In another aspect, the cell endogenously expresses a processing-deficient prelamin A protein. In one aspect, the cell is selected from a cardiac myocyte and a skeletal myocyte. In another aspect, the cell is a prelamin A processing deficient cell that has been isolated from a patient, wherein the cell expresses a prelamin A protein comprising a mutation (with respect to SEQ ID NO:4) selected from: Arg60Gly, Leu85Arg, Glu203Gly, Arg89Leu, Asn19LysAsn195Lys, and Arg377His.

On page 10, please replace the paragraph spanning lines 11-26 with the following amended paragraph:

Another embodiment of the invention relates to a processing deficient prelamin A peptide. The processing deficient prelamin A peptide consists essentially of an amino acid sequence that differs from SEQ ID NO:4 by at least one substitution, deletion or insertion that results in a decrease in a prelamin A or prelamin A pre peptide biological activity selected from: (a) prelamin A processing to release a prelamin A pre peptide consisting of SEQ ID NO:2 or a biologically active homologue thereof; (b) prelamin A pre peptide signal transduction; (c) synchronization of intercellular signaling with changes in lamin A localization and nuclear lamina morphology that occur early in myoblast differentiation; (d) synchronization of transcriptional regulation of muscle-specific genes or cell cycle arrest that occurs concomitant with myoblast differentiation; (e) formation of normal nuclear lamina structure; and/or (f) induction of myoblast activation and differentiation. In one aspect, the processing deficient prelamin A peptide consists essentially of an amino acid sequence that differs from SEQ ID NO:4 by a substitution of an amino acid residue in SEQ ID NO:4 selected from: Arg60, Leu85, Glu203, Arg89, Asn195, Arg377, Tyr646, G649, N650, P653, R654, P658, Q659, N660, Cys661, S662, I663 and M664. In another aspect, the substitution is selected from: Arg60Gly, Leu85Arg, Glu203Gly, Arg89Leu, Asn19LysAsn195Lys, and Arg377His.

On page 11, please replace the paragraph spanning lines 2-3 with the following amended paragraph:

~~Fig. 1 is a Figs. 1A and 1B are digitized image images of an analysis a Western blot for of prelamin A GFP-fusion proteins identified using anti-GFP antibody (Fig. 1A) and anti-prelamin A antibody (Fig. 1B) protein expression and processing.~~

On page 37, please replace the paragraph spanning lines 10-19 with the following amended paragraph:

In another aspect of the invention, it is desirable to produce a homologue of prelamin A that is processing deficient. In this aspect, preferred amino acid residues for modification include, but are not limited to (with reference to SEQ ID NO:4), any residues that are rarely substituted across species, Arg60, Leu85, Glu203, Arg89, Asn195, Arg377, Tyr646, G649, N650, P653, R654, P658, Q659, N660, Cys661, S662, I663 and/or M664. It is to be understood that modifications are not limited to these positions of SEQ ID NO:4, as one of skill in the art will readily be able to select other positions that are likely to tolerate at least a conservative amino acid substitution, if not moderate to any amino acid substitution. In one aspect, the amino acids are substituted for different amino acid residues as follows: Arg60Gly, Leu85ArgLeu85Arg, Glu203Gly, Arg89Leu, Asn19LysAsn195Lys, and Arg377His.

On page 42, please replace the paragraph spanning lines 3-23 with the following amended paragraph:

Another embodiment of the invention relates to a processing deficient prelamin A peptide, wherein the processing deficient prelamin A peptide consists essentially of an amino acid sequence that differs from SEQ ID NO:4 (or a functional allelic variant thereof) by at least one substitution, deletion or insertion that results in a decrease in a prelamin A or prelamin A pre peptide biological activity. Such activity can include, but is not limited to: (a) prelamin A processing to release a prelamin A pre peptide (e.g., SEQ ID NO:2 or a biologically active homologue thereof); (b) prelamin A pre peptide signal transduction; (c) synchronization of intercellular signaling with changes in lamin A localization and nuclear lamina morphology that occur early in myoblast differentiation; (d) synchronization of transcriptional regulation of muscle-specific genes or cell cycle arrest that occurs

concomitant with myoblast differentiation; (e) formation of normal nuclear lamina structure; and (f) induction of myoblast activation and differentiation. In one embodiment, the processing deficient prelamin A peptide consists essentially of an amino acid sequence that differs from SEQ ID NO:4 by a substitution of an amino acid residue in SEQ ID NO:4 selected from the group of: any amino acid that is rarely (e.g., less than 20% of the time) substituted across species, or Arg60, Leu85, Glu203, Arg89, Asn195, Arg377, Tyr646, G649, N650, P653, R654, P658, Q659, N660, Cys661, S662, I663 and/or M664. In another embodiment, the substitution is selected from the group of: Arg60Gly, Leu85ArgLeu85Arg, Glu203Gly, Arg89Leu, Asn19LysAsn195Lys, and Arg377His. Also encompassed by the invention are isolated cells transfected with any of the processing deficient prelamin A proteins described herein.

On page 79, please replace the paragraph spanning lines 11-23 with the following amended paragraph:

The GFP fusion protein containing the Arg89Leu mutation (Fig. 1A, lane 7) has reduced mobility as compared with the other protein constructs. This protein also migrates slower on Western blots of total protein isolated from H9C2 rat cardiac myoblast transfectants probed with the anti-GFP antibody, and from HeLa cell transfectants probed with an anti-lamin A/C antibody (data not shown). In order to confirm the Arg89Leu mutation is affecting prelamin A processing, Western blot analysis of the C2C12 protein extracts was performed using an antibody which specifically recognizes the C-terminal “pre” peptide of prelamin A. Prelamin A ~~prelamin A~~ was detected in the protein extracts from transfectants expressing the Arg89Leu mutation (Fig. 1B, lane 7), and in extracts from cells expressing the Glu203Gly and Arg377His mutations as well (Fig. 1B, lanes 7 and 8, respectively). Furthermore, the prelamin A protein containing the Glu203Gly mutation has a greater mobility than those containing the Arg89Leu and Arg377His mutations,

*Application No. 10/803,541*

demonstrating that the Glu203Gly mutation affects a different prelamin A processing step.